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ABSTRACT:

5 This invention relates to modified pneumolysin polypeptides that retain the immunogenic nature of pneumolysin but have reduced or undetectable hemolytic activity compared to native pneumolysin. The invention also provides a method for generating novel pneumolysin variants with these desired characteristic properties. The invention also provides immunogenic compositions useful as pharmaceutical compositions including vaccines
10 in which non-toxic, modified pneumolysin is used to stimulate protective immunity against *Streptococcus pneumoniae*. The vaccines may be compositions in which the modified pneumolysin is conjugated to bacterial polysaccharides or may be carried on an attenuated viral
15 vector. In addition, the invention also provides a method of using the non-toxic, modified pneumolysin toxoid in order to stimulate antibodies against *Streptococcus pneumoniae* in a treated individual which are then isolated and transferred to a second individual, thereby conferring
20 protection against *Streptococcus pneumoniae* in the second individual.